

OCT 01 2004

REPLACEMENT SHEET

**FIGURE 1A**

Human G Protein Coupled Receptor Family  
 (Receptors known as of January, 1999)

CLASS	LIGAND	NUMBER	TISSUE	PHYSIOLOGY	THERAPEUTICS
•Class I Rhodopsin like	•Amine •Acetylcholine (muscarinic & nicotinic)	5	Brain, Nerves, Heart	Neurotransmitter	Acuity, Alzheimer's
	•Adrenoceptors	6	Brain, Kidney, Lung	Glucogenesis	Diabetes, Cardiovascular
	•Alpha Adrenoceptors	3	Kidney, Heart	Muscle Contraction	Cardiovascular, Respiratory
	•Beta Adrenoceptors	5	Brain, Kidney, GI	Neurotransmitter	Cardiovascular, Parkinson's
	•Dopamine	2	Vascular, Heart, Brain	Vasular Permeability	Anti-inflammatory, Ulcers
	•Histamine	16	Most Tissues	Neurotransmitter	Depression, Insomnia, Analgesic
	•Serotonin (5-HT)				
	•Peptide	2	Vascular, Liver, Kidney	Vasoconstriction	Cardiovascular, Endocrine
	•Angiotensin	1	Liver, Blood	Vasodilation,	Anti-inflammatory, Asthma
	•Bradykinin	1	Blood	Immune System	Anti-inflammatory
	•C5a anaphylatoxin	3	Blood	Chemoattractant	Anti-inflammatory
	•Fmet-leu-phe	1	Blood	Chemoattractant	Anti-inflammatory
	•Interleukin-8	6	Blood	Chemoattractant	Anti-inflammatory
	•Chemokine	2	Brain	Fat Metabolism	Obesity
	•Orexin	1	Brain	Bronchodilator, Pain	Airway Diseases, Anesthetic
	•Nociceptin	2	Gastrointestinal	Motility, Fat Absorption	Gastrointestinal, Obesity, Parkinson's
	•CCK (Gastrin)	2	Heart, Bronchus, Brain	Muscle Contraction	Cardiovascular, Respiratory
	•Endothelin	5	Kidney, Brain	Metabolic Regulation	Anti-inflammatory, Analgesics
	•Melanocortin	5	Nerves, Intestine, Blood	Neurotransmitter	Behavior, Memory, Cardiovascular
	•Neuropeptide Y	1	Brain,	CNS	Cardiovascular, Analgesic
	•Neurotensin	3	Brain,	CNS	Depression, Analgesic
	•Opioid	5	Brain, Gastrointestinal	Neurotransmitter	Oncology, Alzheimer's
	•Somatostatin				
	•Tachykinin	3	Brain Nerves	Neurohormone	Depression, Analgesic
	(Substance P, NKA <sub>1</sub> )				



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**FIGURE 1B**

•Thrombin	3	Platelets, Blood Vessels	Coagulation	Anti-coagulant, Anti-inflammatory
•Vasopressin-like	4	Arteries, Heart, Bladder	Water Balance	Anti-diuretic, Diabetic Complications
•Galanin	1	Brain, Pancreas	Neurotransmitter	Analgesics, Alzheimer's
•Hormone protein				
•Follicle stimulating hormone	1	Ovary, Testis	Endocrine	Infertility
•Lutropin-choriogonadotropin	1	Ovary, Testis	Endocrine	Infertility
•Thyrotropin	1	Thyroid	Endocrine	Thyroidism, Metabolism
•(Rhod)opsin				
•Opsin	5	Eye	Photoreception	Ophthalmic Diseases
•Olfactory	4 (~1000)	Nose	Smell	Olfactory Diseases
•Prostanoid				
•Prostaglandin	5	Atrial, Gastrointestinal	Vasodilation, Pain	Cardiovascular, Analgesic
•Lysophosphatidic Acid	2	Vessels, Heart, Lung	Inflammation	Cancer, Anti-Inflammatory
•Sphingosine-1-phosphate	2	Most Cells	Cell proliferation	Cancer
•Leukotriene	1	White Blood Cells, Bronchus	Inflammation	Asthma, Rheumatoid Arthritis
•Prostacyclin	1	Arterial, Gastrointestinal	Platelet Regulation	Cardiovascular
•Thromboxane	1	Arterial, Bronchus	Vasoconstriction	Cardiovascular, Respiratory
•Nucleotide-like				
•Adenosine	4	Vascular, Bronchus	Multiple Effects	Cardiovascular, Respiratory
•Purinoceptors	4	Vascular, Platelets	Relaxes Muscle	Cardiovascular, Respiratory
•Cannabis	2	Brain	Sensory Perception	Analgesics, Memory
•Platelet activating factor	1	Most Peripheral Tissues	Inflammation	Anti-inflammatory, Anti-asthmatic
•Gonadotropin-releasing hormone like				
•Gonadotropin-releasing hormone	1	Reproductive Organs, Pituitary	Reproduction	Prostate Cancer, Endometriosis
•Thyrotropin-releasing hormone	1	Pituitary, Brain	Thyroid Regulation	Metabolic Regulation
•Growth hormone-inhibiting factor	1	Gastrointestinal	Neuroendocrine	Oncology, Alzheimer's
•Melatonin	1	Brain, Eye, Pituitary	Neuroendocrine	Regulation of Circadian Cycle
•Class II				
Secretin like				
•Secretin	1	Gastrointestinal, Heart	Digestion	Obesity, Gastrointestinal
•Calcitonin	1	Bone, Brain	Calcium Resorption	Osteoporosis
•Corticotropin releasing factor/tuocortin	1	Adrenal, Vascular, Brain	Neuroendocrine	Stress, Mood, Obesity
•Gastric inhibitory peptide (GIP)	1	Adrenals, Fat Cells	Sugar/Fat Metabolism	Diabetes, Obesity
•Glucagon	1	Liver, Fat Cells, Heart	Gluconeogenesis	Cardiovascular

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**FIGURE 1C**

•Glucagon-like Peptide 1 (GLP-1)	1	Pancreas, Stomach, Lung	Gluconeogenesis
•Growth hormone-releasing hormone	1	Brain	Neuroendocrine
•Parathyroid hormone	1	Bone, Kidney	Calcium Regulation
•PACAP	1	Brain, Pancreas, Adrenals	Metabolism
•Vasoactive intestinal polypeptide (VIP)	1	Gastrointestinal	Motility
•Metabotropic Glutamate	7	Brain	Sensory Perception
•GABA <sub>B</sub>	1	Brain	Neurotransmitter
•Extracellular Calcium Sensing	1	Parathyroid, Kidney, GI Tract	Calcium Regulation

•Class III



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**FIGURE 2A**

**G protein-coupled receptors:**

(Division into Class A  
Or Class B)

1. **A1 adenosine receptor [Homo sapiens]. ACCESSION AAB25533**  
npiwyaf riqkfrvtfl kiwndhfrcq pappidedlp eerpdd  
**Class A**
2. **adrenergic, alpha -1B-, receptor [Homo sapiens]. ACCESSION NP\_000670**  
npiiytypc sskefkrafv rilgcqcrgr grrrrrrrrr lggcaytyrp wtrggslers qsrkdsldds gsclsgsqr  
lpsaspypg lrggapppv e lcafpewkap gallslape ppgrgrhds gplftfkllt epespgtdgg asnggceaaa  
dvangqpgf s nmp lapqgf  
**Class A**
3. **adrenergic receptor alpha-2A [Homo sapiens]. ACCESSION AAG00447**  
npiyti fn hdfrrafkki lcrgdrkriv  
**Class A**
4. **alpha-2B-adrenergic receptor - human. ACCESSION A37223**  
npiyti fn qdftraftri lcrpwtqtaw  
**Class A**
5. **alpha-2C-adrenergic receptor - human. ACCESSION A31237**  
npiytvfn qdfrpsfkhi lfrtttrgfr q  
**Class A**
6. **beta-1-adrenergic receptor [Homo sapiens]. ACCESSION NP\_000675**  
npiiycrsp pdfkrafqgl lccarraarr rhathgdrpr asgclarpgp ppspgaasdd ddddvvvgatp parllepwag  
cnggaaadsd ssldepcrpg faseskv  
**Class A**
7. **beta-2 adrenergic receptor. ACCESSION P07550**  
npliycrsp dfriafqell clrsslkay gngyssngnt 361 geqsgyhveq ekenklced lpgtedfvgh qgtvpsdnid  
sqgrncstnd sll  
**Class A**
8. **dopamine receptor D1 [Homo sapiens]. ACCESSION NP\_000785**  
npii yafnadfrka fstllgcyl cpatnnaiet vsinnngaam fsshheprgs iskecnlvyl iphavgssed  
lkkeeaaagia rpleklspal svildytdv slekiqpitq ngqhpt  
**Class A**
9. **D(2) dopamine receptor. ACCESSION P14416**  
npiytfm iefrkafkli lhc  
**Class A**

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**FIGURE 2B**

10. **d3 dopamine receptor - human.** ACCESSION G01977  
 np viytfnief rkafkilsc  
**Class A**

11. **dopamine receptor D4 - human.** ACCESSION DYHUD4  
 npviytv fnaefrnvfr kalracc  
**Class A**

12. **dopamine receptor D5 - human.** ACCESSION DYHUD5  
 npviya fnadfqkvfa qllgcshfcs rtpvetvnis nelisynqdi vfhkeiaay ihmmpnavtp gnrevdndee  
 egpfdrmfqj yqtspdgdpv aesvweldce geisldkitp ftpngfh  
**Class A**

13. **muscarinic acetylcholine receptor M1 [Homo sapiens].** ACCESSION NP\_000729  
 npmcyal cnkafrdtfr lllcrwdkr rwrkipkrpg svhrtprqc  
**Class A**

14. **muscarinic acetylcholine receptor M2 [Homo sapiens].** ACCESSION NP\_000730  
 npacy alcnatfkkt fkhlmcchyk nigatr  
**Class A**

15. **muscarinic acetylcholine receptor M3 [Homo sapiens].** ACCESSION NP\_000731  
 n pvcyalcnkt frtfkmlll cqcdkkrrk qqyqqrqsvi fhkrapeqal  
**Class A**

16. **muscarinic acetylcholine receptor M4 [Homo sapiens].** ACCESSION NP\_000732  
 npa cyalcnatfk ktfrhlllcq yrnigtar  
**Class A**

17. **m5 muscarinic receptor.** locus HUMACHRM ACCESSION AAA51569  
 npicyalcnr tfkfkml1 lcrwkkkkve eklywqgnsk lp  
**Class A**

18. **5-hydroxytryptamine (serotonin) receptor 1A [Homo sapiens].** ACCESSION BAA90449  
 npviy ayfnkdfqna fkkikckf  
**Class A**

19. **5-hydroxytryptamine (serotonin) receptor 1B [Homo sapiens].** ACCESSION BAA94455  
 npiiyt msnedfkqaf hklirfkcts  
**Class A**

20. **5-hydroxytryptamine (serotonin) receptor 1E [Homo sapiens].** ACCESSION BAA94458  
 n pllytsned fklafkkir cre  
**Class A**

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**FIGURE 2C**



21. **OLFACTOORY RECEPTOR 6A1.** ACCESSION O95222  
npiiyclrnq evkralccil hlyqhqdpp kkgsvnv  
**Class A**
22. **OLFACTOORY RECEPTOR 2C1.** ACCESSION O95371  
npliy tlrmnevkg a lrrllgkgre vg  
**Class A**
23. **angiotensin receptor 1 [Homo sapiens].** ACCESSION NP\_033611  
npl fyglgkkfk ryflqlkyi ppkakhsnl skmsfsyrs pdnvssstik kpapcfeve  
**Class B**
24. **angiotensin receptor 2 [Homo sapiens].** ACCESSION NP\_000677  
npflycf vgnrfqqkrlr svfrvpitwl qgkresmscr kssslremet fvs  
**Class B**
25. **interleukin 8 receptor beta (CXCR2) [Homo sapiens].** ACCESSION NM\_001557  
NPLIYAFIGQKFRHGLLKI LAI HGLISKDSL PKDSRPSFVGSSSGHTSTTL  
**Class B**
26. **cx3c chemokine receptor 1 (cx3cr1) (fractalkine receptor)**  
ACCESSION P49238  
np liyafagekf rrylyhlygk clavlcgrsv hvdfsssesq rsrhgsvlss nftyhtsdgd allll  
**Class B**
27. **neurotensin receptor - human.** ACCESSION S29506  
n pilynlvsan frhiflatla clcpvwrrrr krpafsrkad svssnhfss natretly  
**Class B**
28. **SUBSTANCE-P RECEPTOR (SPR) (NK-1 RECEPTOR) (NK-1R).** ACCESSION P25103  
npiiyccld rfrlgfkhafrccpfisagd yeglemkstr ylqtqgsvyk vsrlettistvvgahheepe dgpkatpssl  
dltsncssrs dsktmtesfs fssnvls  
**Class B**
29. **vasopressin receptor type 2 [Homo sapiens].** ACCESSION AAD16444  
npwiyasfss svsselrsll ccargrtpps lgpqdesctt assslakdts s  
**Class B**
30. **thyrotropin-releasing hormone receptor - human.** ACCESSION JN0708  
npyiy nlmsqkfraa frklcnckqk ptekpanysv alnysvikes dhfstelddi tvtdtysat kvsfddtcla sevsfsqs  
**Class B**
31. **oxytocin receptor - human.** ACCESSION A55493  
npwiymlftghlfhel vqrflccas ylkgrrlget saskksnsss fvishrsssq rscsqpsta  
**Class B**



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**FIGURE 2D**

32. **neuromedin U receptor [Homo sapiens].** ACCESSION AAG24793  
npylyslmssrfretfqealclgacchrlrprhsshlsrmittgstlcvgsglgswvhplagndpeaqqetdps  
**Class B**

33. **gastrin receptor.** ACCESSION AAC37528  
nplvy cfmhrrfrqa cletcarccp rpprarpral pdedpptpsi aslsrlsytt isflgpg  
**Class B**

34. **galanin receptor 3 [Homo sapiens].** ACCESSION 10879541  
nplv yalasrhfra rfrrlwpcgr rrhrarral rrvrpassgp pgcpgdarps grllagggqg pepregpvhg geaargpe  
**Class A**

35. **edg-1 - human.** ACCESSION A35300  
npiiy tlnkemrra firimscckc psgdsagkfk rpiagmefs rsksdnsshp 361 qkdegdnpet imssgnvnss s  
**Class A**

36. **central cannabinoid receptor [Homo sapiens].** ACCESSION NP\_057167  
npiiyalr skdlrhafrs mfpscegtaq pldnsmgdsd clkhannaa svhraaesci kstvkiakvt msvstdtsae al  
**Class A**

37. **delta opioid receptor - human.** ACCESSION I38532  
npylyaf ldenfkrcfr qlcrkpcgrp dpssfsrpreatarervtac tpsdgpgggr aa  
**Class A**

38. **proteinase activated receptor 2 (PAR-2) human.** ACCESSION P55085  
dpfvyyfvshdfrdhaknallcrsvrtvkqmqvsltskkhsrkssyssssttvktsy  
**Class A**

39. **vasopressive intestinal peptide receptor (VIPR) rat.** ACCESSION NM\_012685  
NGEVQAEIIRRKWRRWHLQGVLGWSSKSQHPWGGSNGATCSTQVSMLTRVSPSARR  
SSSFQAEVSLV  
**Class B**

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## FIGURE 3A

**Human V2R DNA (nucleotides encoding the last 29 amino acids of the V2R and the adjacent stop codon):**

**gcccggggacgcacccacccagcctgggtccccaaagatgagtctgcaccaccgcccagtcct**  
**ccctggccaaggacacttcatcgta**

## FIGURE 3B

**PCR amplified human V2R DNA fragment:**

**gcggccgcacggggacgcacccacccagcctgggtccccaaagatgagtctgcaccaccgccc**  
**agctcctccctggccaaggacacttcatcgtaagatctccgcggtctaga**

\*Additions and changes to the V2R DNA are underlined.

\*The Sma I (cccggg) restriction enzyme site (underlined in Fig. 3A) was eliminated in the amplified DNA fragment by changing a cytosine to an adenine.

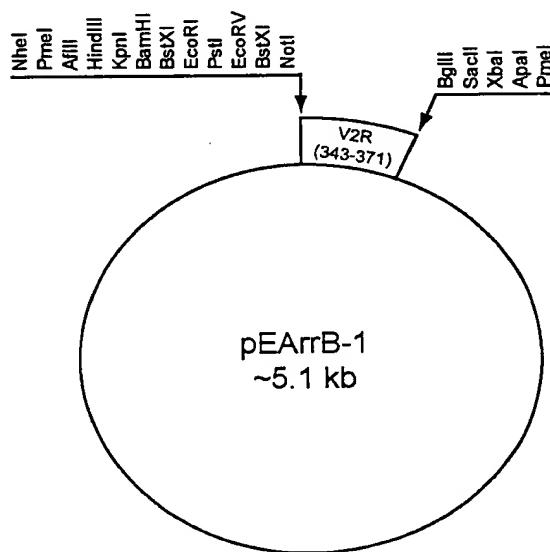
\*A Not I restriction site (gcggccgc) was incorporated into the amplified DNA fragment by adding 6 nucleotides (gcggcc) to the 5' end of the V2R DNA.

\*Bgl II (agatct), Sac II (ccgcgg), and Xba I (tctaga) restriction enzyme sites were added to the 3' end of the V2R DNA.

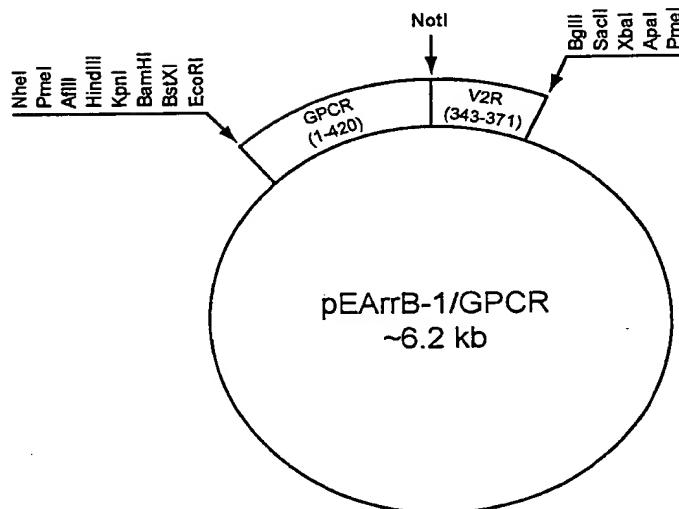


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**FIGURE 4A**



**FIGURE 4B**



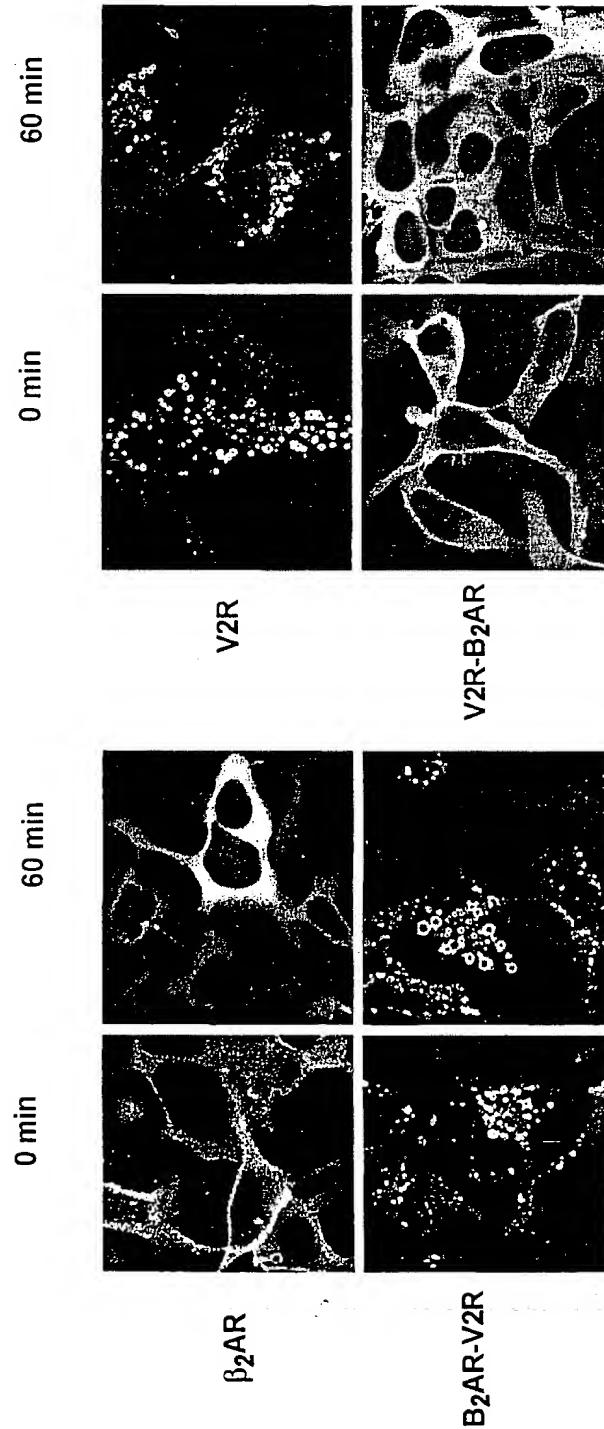
**FIGURE 4C**

...AAARGRTPPSLGPQDESCTTASSSLAKDTSS



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FIGURE 7A  
FIGURE 7B





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**FIGURE 8A**

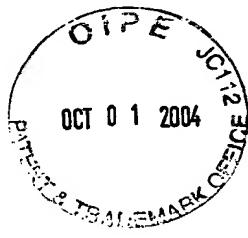
1) V2R	CARGRTPPSLGPQDESCTTASSSLAKDTSS
2) V2R-S362X	CARGRTPPSLGPQDESCTTA
3) V2R-SSSTSS/AAAAAA	CARGRTPPSLGPQDESCTTAA <u>AAALAKDAAA</u>
4) V2R-TSS/AAA	CARGRTPPSLGPQDESCTTASSSLAKD <u>AAA</u>
5) V24-SSS/AAA	CARGRTPPSLGPQDESCTTAA <u>AAALAKDTSS</u>
6) β <sub>2</sub> AR-V2R-SSS/AAA	CARGRTPPSLGPQDESCTTAA <u>AAALAKDTSS</u>
7) β <sub>2</sub> AR	CLRRSSLKAYGNGYSSNGNTGEQSGYHVEQEKENKLLCEDLP- GTEDFVGHQGTVPSDNIDSQGRNCSTNDSLL
8) β <sub>2</sub> AR413-V2R10	CLRRSSLKAYGNGYSSNGNTGEQSGYHVEQEKENKLLCEDLP- GTEDFVGHQGTVPSDNIDSQGRNCSTNDSLL <u>SSSLAKDTSS</u>
9) β <sub>2</sub> AR360-V2R10	CLRRSSLKAYGNGYSSNGNT <u>SSSLAKDTSS</u>

**FIGURE 8B**

V2R	NPWIYASFSSSVSELRSLLCCARGRTPPSLGPQDESCTT <u>ASSSLAKDTSS</u>
AAA-1	----- <u>AAA</u> -----
AAA-2	----- <u>AAA</u> -----
NTR-1	NPILYNLVSANFRQVFLSTLACLCPGWRHRRKKRPTFSRKPN <u>MSNNHAFSTSATRELY</u>
AMAA	----- <u>A-AA</u> -----
AAA	----- <u>AAA</u> -----
OTR	NPWIYMLFTGHLFHELVQRFLCCSASYLKGRRLGET <u>SASKSNSSSFVLSHRSSQRSCSQPSTA</u>
AAAA	----- <u>AAAA</u> -----
AAA-1	----- <u>AAA</u> -----
AAA-2	----- <u>AAA</u> -----

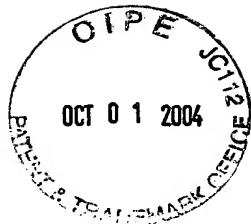
REPLACEMENT SHEET

**FIGURE 8C**



NPIIYCCLANDRFRIGFKHAFRCCPFISAGDYEGLEMKSTRYLQTOGVYKVSRLETTISTVVGAEHEEEPEDGPKATPSSLKLTNCSSRSDSKTMTESSSNVLS  
-X-----X  
383X  
355X  
325X  
AA-AA  
A-AA  
APAA

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## FIGURE 9A

### Amino Acid Sequence of the Wild-Type Receptors

#### Amino acid sequence of the wild-type V2R

MLMASTTSAVPGHPSLPSLPSNSSQERPLDTRDPLLARAELALLSIVFVAVALSNGLVLAALARRGRGHWAPIHVFIGHLCLADLAVALFQVLQPQLAWKATDRFRGPDALCRAVKYLQMVGMYASSYMIAMTLDRHRAICRPMLAYRHGSGAHWNRPVLVAWAFLSLLSLPQLFIFAQRNVEGGSGVTDCWACFAEPWGRRTYVTWIALMVFVAPTLGIAACQVLIFREIHASLVPGPSERPGRGGRRRTGSPGEGAHVSAAVAKTVRMTLVIVVVYVLCWAPFFLVQLWAAWDPEAPLEGA  
**P**FVLLMILLASLNSCTNPWIYASFSSSVSSELRSLLCC**A**RGRTPPSLGPQDESCTTASSLA  
**K**DTSS

(Seq. ID No. 1)

## FIGURE 9B

#### Amino acid sequence of the wild-type $\beta_2$ AR

MGQPGNGSAFLLAPNRSHAPDHDTQQRDEVVVVGIGIVMSLIVLAIIVFGNVLVITAIAKFERLQTVTNYFITSACADLVMGLAVVPFGAAHILMKMWTFGNFCEFWTSIDVLCVTASIELTCVIAVDRYFAITSPIFYQSLLTKNKARVIIIMVWIVSGLTSFLPIQMHWYRATHQEAINCYANETCCDFFTNQAYAIASSIVSFYVPLVIMVFVYSRVFQEAKRQLQKIDKSEGRFHVQNLSQVEQDGRTGHGLRRSSKFCLKEHKALKTLGIIMGTFTLCWLPFFIVNIVHVIQDNLIRKEVYILLNWIGYVNSGFNPLIYCRSPDFRIAFQELLCLRRSSLKAYGNGYSSNGNTGEQSGYHVEQEKENKLLCEDLPGTEDFVGHQGTVPSDNIDSQGRNCSTNDSSL

(Seq. ID No. 2)

## FIGURE 9C

### Amino Acid Sequence of the Chimeric Receptors

#### Amino acid sequence of the $\beta_2$ AR-V2R chimera (Oakley et al.)

MGQPGNGSAFLLAPNRSHAPDHDTQQRDEVVVVGIGIVMSLIVLAIIVFGNVLVITAIAKFERLQTVTNYFITSACADLVMGLAVVPFGAAHILMKMWTFGNFCEFWTSIDVLCVTASIELTCVIAVDRYFAITSPIFYQSLLTKNKARVIIIMVWIVSGLTSFLPIQMHWYRATHQEAINCYANETCCDFFTNQAYAIASSIVSFYVPLVIMVFVYSRVFQEAKRQLQKIDKSEGRFHVQNLSQVEQDGRTGHGLRRSSKFCLKEHKALKTLGIIMGTFTLCWLPFFIVNIVHVIQDNLIRKEVYILLNWIGYVNSGFNPLIYCRSPDFRIAFQELL**C**ARGRTPPSLGPQDESCTTASSLA  
**DTSS**

(Seq. ID No. 3)

\*shown in bold are the amino acids that were moved to the  $\beta_2$ AR to increase its affinity for arrestin.



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**FIGURE 10A**

**Amino acid sequence of the MOR-V2R chimera expressed from the pEArrB-1/MOR vector**

MDSSTGPGNTSDCSDPLAQASCSPAPGSWLNLSHV DGNQSDPCGLNRTGLG  
GNDSLCPQTGPSMVTAITIMALYSIVCVVGLFGNFLVMYVIVRYTKMKTA  
TNIYIFNLALADALATSTLPFQS VNYLMGTWPFGTILCKIVISIDYYNMFT  
SIFTLCMSVDRYIAVCHPVKALDFRTPRNAKIVNVCNWILSSAIGLPVMF  
MATTKYRQGSIDCTLTFSHPTWYWE NLLKICVFIFAFIMPILIIITVCYGLM  
ILRLKSVRMLSGSKEKDRNLRRI TRMVLVVVAVFIVCWTPHIYVI KALI  
TIPETTFQTVWHFCIALGYNSCLNPVLYAFLDENFKRCFREFCAAARGR  
**TPPSLGPQDESCTTASSSLAKDTSS**

(Seq. ID No. 4)

**FIGURE 10B**

**Amino acid sequence of the D1AR-V2R chimera expressed from the pEArrB-1/D1AR vector**

MAPNTSTMDEAGLPAERDFSFRILTACFLSLLILSTLLGNTLVCAAVIRFR  
HLRSKVNFVISLAVSDLLVAVLVMPWKAVAEIAGFWPFGSFCNIWVAFD  
IMCSTASILNLCVISVDRYWAISSPFQYERKMTPKAAFILISVAWTLSVLI  
SFIPVQLSWHKAKPTWPLDGNFTSLEDTEDDNCDTRLSRTYAISSSLISFY  
IPVVAIMIVTYTSIYRIAQKQIRRISALERA AVHAKNCQTTAGNGNPVECAQ  
SESSFKMSFKRET KVLKTL SVIMGVFVCCWL PFFISNCMVPFCGSEETQPF  
CIDSITFDVFWFGWANSSLNPIIYAFNADFQKAFSTLLGCYRLCAAARGR  
**TPPSLGPQDESCTTASSSLAKDTSS**

(Seq. ID No. 5)



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## FIGURE 10C

**Amino acid sequence of the 5HT1AR-V2R chimera expressed from the pEArrB-1/5HT1AR vector**

MDVLSPGQGNNTSPPAPFETGGNTTGISDVTVSYQVITSLLLGTIFCAV  
LGNACVVAIAALERSLQNVANYLIGSLAVTDLMSVLVLPMALYQVLNKW  
TLGQVTCDFIALDVLCCTSSILHLCAIALDRYWAITDPIDYVNKRTPRRA  
AALISLTWLIGFLISIPPMLGWRTPEDRSDPDACTISKDHGYTIYSTFGAF  
YIPLLMLVLYGRIFRAARFRIRKTVKKVEKTGADTRHGASPAQPDKSVN  
GESGSRNWRLLGVESKAGGALCANGAVRQGDDGAALEVIEVHRVGNSKEHLP  
LPSEAGPTPCAPASFERKNERNAEAKRMALARERKTVKTLGIIMGTFLC  
WLPFFIVALVLPFCESSCHMPTLLGAI  
INWLGYNSNLLNPVIYAYFNKFQNAFKKIIKCNFCAAARGRTPPSLGPQD  
**ESCTTASSSLAKDTSS**

(Seq. ID No. 6)

## FIGURE 10D

**Amino acid sequence of the β3AR-V2R chimera expressed from the pEArrB-1/β3AR vector**

MAPWPHENSSLAPWPDLPTLAPNTANTSGLPGVPWEAALAGALLALAVLAT  
VGGNLLVIVAIAWTPRLQTMTNVFTVTSLAAADLVMGLLVVPPAATLALTGH  
WPLGATGCELWTSVDVLCVTASIETLCALAVDRYLAUTNPLRYGALVTKRC  
ARTAVVLLVVVSAAVSFAPIMSQWWRGADAEAQRCHSNPRCCAFASNMPY  
VLLSSSVSFYLPLLVMLFVYARVFVVATRQLRLRGELGRFPPEESPPAPS  
RSLAPAPVGTCAAPPEGVPACGRRPARLLPLREHRALCTLGLIMGTFTLCWL  
PFFLANVLRALGGPSLVPGP AFLALNWLGYANSAFNPLIYCRSPDFRSAFR  
**RLLCRCAAARGRTPPSLGPQDESCTTASSSLAKDTSS**

(Seq. ID No. 7)

## FIGURE 10E

**Amino acid sequence of the Edg1R-V2R chimera expressed from the pEArrB-1/Edg1R vector**

MGPTSVPLVKAHRSSVSDYVNYDIIVRHYNYTGKLNISADKENSIKLTSVV  
FILICCFIILENIFVLLTIWKTKKFHRPMYYFIGNLALS DLLAGVAYTANL  
LLSGATTYKLTPAQWFLREGSMFVALSASVFSLLAIAIERYITMLKMKLHN  
GSNNFRLFLLISACWVISLILGGLPIMGWNCISALSSCSTVLPYHKHYIL  
FCTTVFTLLLLSIVILYCRYSLVRTRSRLTFRKNISKASRSSEKSLALL  
KTVIIVLSVFIACWAPLFILLLDVGCKVKTCDILFRAEYFLVAVLNSGT  
NPIIYTLTNKEMRRAFIRIMSCCKCAAARGRTPPSLGPQDESCTTASSSLA  
**KDTSS**

(Seq. ID No. 8)



## **REPLACEMENT SHEET**

## **FIGURE 11A**

## Nucleotide sequence of the $\beta$ 2AR-V2R chimera

atggggcaaccggaaacggcagcgccctttgtggcacccaatagaaggccatgcgccggacc  
acgacgtcacgcagcaaaggacgagggtgtgggtggcatggcatcgcatgtctctcat  
cgtcctggccatcggtttggcaatgtgtcatcacagccattgccaagttcgagcgtctg  
cagacggtaccaactacttcattcaactggtgtgtgtgtgtgtgtgtgtgtgtgtgtgt  
tggtgcccttggggcccccatttttatgaaaatgtggactttttggcaacttctgggtgcga  
gttttgacttccattgtatgt  
gtggatcgctactttgccattacttcaccttcaagtaccagagactgctgaccagaataagg  
cccgggtgatcattctgtatgggtgtggattgtgtcaggccttaccccttcttgcaccattcagat  
gcacttgttacccggccacccaccaggaaagccatcaactgtatgccaatgagacctgctgtgac  
ttttcacgaaccaagcctatgccattgcctttccatcggttttttttttttttttttttttttt  
tcatggtctcgctactccagggtcttcaggaggccaaaaggcagctccagaagattgacaa  
atctgagggcccttccatgtccagaaccttagccaggtggagcaggatggcggacggggcat  
ggactccgcagatcttccaagttctgtgtgaaggagcacaagccctcaagacgtttaggcatca  
tcatggcacttccacccctgt  
ggataaacctcatccgttaaggaagttacatccctctaaattggataggctatgtcaattctgg  
ttcaatcccccttatctactgccggagccagattcaggattgcctccaggagcttctgtgcg  
cccggggacgcaccccacccagccatgggtccccaaagatgagtcctgcaccaccgcccagctc  
cctggccaaggacacttcattcatcgta

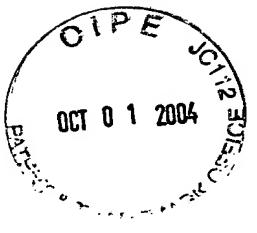
(SEQ ID No. 9)

## FIGURE 11B

## Nucleotide sequence of the MOR-V2R chimera

atggacagcagcaccggcccagggAACACCCAGCGACTGCTAGACCCCTAGCTCAGGGCAAGTT  
gctccccagcacctggctcctggctcaacttgtccacgttgcataaccaggatccatgcgt  
cggtctgaaccgcaccgggcttggcgaaacgcacagcgcctgtgccctcagaccggcagcccttc  
atggtcacagccattaccatcatggccctctactctatcggtgttagtgggcctttcggaa  
acttcctggcatgtatgtgatttaagatacacaaaaatgaagactgccaccacatctacat  
tttcaaccttgctcggcagacgccttagcgaccagtacactgcccttcagagtgtcaactac  
ctgatggaaacatggcccttcgaaaccatcctctgcaagatcgatctcaatagattactaca  
acatgttaccaggatattcacccctcgaccatgagcggtggaccgctacattgtgtctgcca  
cccagtcaaaggccctggattccgtaccccccggaaatgcaaaatcgtaacgtctgcaactgg  
atcctctcttcgcatcggtctgcctgtaatgttcatggcaaccacaaaatacaggcagggt  
ccatagattgcaccctcacgttcccaccaacctggtaactgggagaacctgctcaaatctg  
tgtcttatctcgcttcatcatgccatcctcatcatactgtgtgttacggccctgatgatc  
ttacgactcaagagcggtcgcatgctatcggtccaaagaaaaggacaggaatctgcgcagga  
tcaccggatgggtctgggtcggtgttattatcgctgtggaccccatccacatcta  
cgtcatcatcaaagcgctgatcacgattccagaaaccacattcagaccgttctggcacttc  
tgcattgcttgggttacacgaacagctgcctgaatccagttttacgccttcctggatgaaa  
acttcaagcgatgcttcagagagttctgcggccgcacggggacgcacccacccacgcctgg  
tccccaaagatgagtcctgcaccaccgcacgtcctccctggccaaggacacttcatcgta  
(SEQ ID No. 10)

(SEQ ID No. 10)



REPLACEMENT SHEET

**FIGURE 11C**

**Nucleotide sequence of the D1AR-V2R chimera**

atggctctaacaacttaccatggatgaggccggctgccagcggagagggatttccctttc  
gcacccatcacggcgttccctgtcactgtcatctgtccactctccctggcaataccctgt  
ctgtgcggccgtcatccgggttcgacacacgtggatccaagggtgaccaacttcttgcacatct  
tttagctgttcagatcttgggtgtccctgtcatgcctggaaagctgtggccgagattg  
ctggctttggcccttgggtcctttgtaacatctggtagcccttgacatcatgtgtctac  
ggcgtccattctgaacctctgcgtgatcagcgtggacaggtaactggctatccagcccttc  
cagtatgagagaaatgacccccaaaggcagcgcattcatccgtattagcgtacatggactctgt  
ctgtccttatccatcccagtaactgtaagctggcacaaggcaagccacatggccctt  
ggatggcaatttacccctggaggacaccgaggatgacaactgtgacacaagggttggcagg  
acgtatgccattcatcgccctcatcagtttacatccccgtagccattatgatcgtcacct  
acaccagtatctacaggattggccagaagaaaaccggcgcatctcagccttgagagggcagca  
gtccatgccaagaattggccagaccaccgcaggtaacgggaaccccgatcgatgcggccagtctg  
aaagttcccttaagatgtcctcaagaggagacgaaagtctaaagacgcgtgtcat  
gggggtgtttgtgtctggctcccttcttcatctcgaactgtatggtgccttctgtggc  
tctgaggagaccgcattctgcattccatcaccttcgatgtgtttgtgtgggttgggt  
ggcgaattctccctgaaccccattattatgctttaatgctgacttccagaaggcgttctc  
aaccctttaggatgctacagactctgcggccgacgggacgcacccacccagcctgggt  
ccccaaatgagtcctgcaccaccgcagtcctccctggccaaggacacttcatcgtga  
(SEQ ID No. 11)

**FIGURE 11D**

**Nucleotide sequence of the 5HT1AR-V2R chimera**

atggatgtgctagccctggtcagggcaacaacaccacatcaccacggctccctttagacccg  
gcggcaacactactggtatctccgacgtgaccgtcagctaccaagtgtacacccatctctgtc  
gggcacgctcatcttcgcgggtctggcaatgcgtgcgtggctgcacatgccttggag  
cgctccctgcagaacgtggccaattatcttattggctttggcggtcaccgcacatgggt  
cggtgttgggtgtccatggcccgctgtatcaggtgctcaacaagtggacactggccagg  
aacctgcacactgttcatcgccctcgacgtgtctgcacccatccatcttgcacctgtgc  
gccatcgcgtggacaggtaactggccatcacggacccatcgactacgtgaacaaggagacgc  
ccggcgccgctgcgtcatctgcgtacttgcgttattggcttcatctatccgc  
catgcgtggctggcgaccccgaaagaccgctggacccgcacgcattagcaaggat  
catggctacactatcttccaccccttggagcttctacatccgcgtctgcacatgcgtgg  
tctatggcgcatattccgagctgcgcgttccgcacccgcacgggtcaaaaagggtggagaa  
gaccggagcggacacccgcattggagcatctccgcggccgcagcccaagaagagtgtgaatgg  
gagtggggagcaggaactggaggctggcggtggagagcaaggctgggggtctctgtgc  
atggcgccgtgaggcaagggtgacgatggcgccgcctggagggtatcgagggtgcacccagg  
caactccaaagagcactgcctgcctgcacccgcacgcaggctggcttgcacccgcct  
ttcgagagaaaaatgagcgcaacgcgcaggcgaagcgcaagatggccctggcccgagag  
agacagtgaagacgcgtggcatcatcatgggcacccatctctgtgtggctgc  
cgtggcttcgttctgccttcgtcgagagcagctgcacatgcacccgcatttgc  
atcaattggctggctactccaactctgtcttaaccccgtcattacgcataacttcaacaagg  
acttcaaaacgcgtttaagaagatcattaagtgtaaacttgcgcggccgcacgggacgcac  
cccacccaggctgggtcccaagatgagtcctgcaccaccgcacccgcac  
acttcatcgtga  
(SEQ ID No. 12)



REPLACEMENT SHEET

**FIGURE 11E**

**Nucleotide sequence of the β3AR-V2R chimera**

atggctccgtggcctcacgagaacagctcttgccccatggccggaccccccaccctggcgc  
ccaataccgccaacaccaggctggctgccagggttccgtggaggcgccctagccggggccct  
gctggcgctggcggtgctggccaccgtgggaggcaacctgtggcatcgccatcgccctgg  
actccgagactccagaccatgaccaacgtttcgacttcgctggccgacgtggccactggccgttggcgc  
tgggactctgggtggccggccacccgtggcgctgactggccactggccgttggcgc  
cactggctgcgagctgtggacccgtggacgtgtgaccggccagcatcgaaaccctg  
tgccgcctggccgtggaccgtggacttggatcgccatcgccatcgccatcgccatcgcc  
ccaaggcgctgcgcccggacagctgtggcttggtgtgggtcggtcgccgcgggtgtcggttc  
gccccatcatgagccagtggtggcgtagggggccacgcccggaggcgacgtggccactccaac  
ccgcgctgctgtgccttcgcctccaacatgcctacgtgctgtgttgcacccgtcggttacggcgactggta  
acccgttgcgttgcgttatcgccatcgccatcgccatcgccatcgccatcgccatcgcc  
gcccgttgcgtgcggggagctggccgtttccggccgagagatctccgcggccgtcgcc  
tctctggcccccggcccccgggtggggacgtgcgtccggccgaaagggtggccctgcccggc  
ggccgc  
cacccgttgcgttgcgttgcgttgcgttgcgttgcgttgcgttgcgttgcgttgcgttgc  
tctcttagtcccgccggccggcttccttgcgttgcgttgcgttgcgttgcgttgcgttgc  
acccgctcatctactgcccgcagccggacttcgcagcgcctccgcgttgcgttgcgttgc  
cgccggccgcacggggacgcacccacccacccctgggtcccaagatgagtcctgcaccaccgcca  
gtcctccctggccaaggacactcatcgta

(SEQ ID No. 13)

**FIGURE 11F**

**Nucleotide sequence of the Edg1-V2R chimera**

atggggcccaccagcgtcccgctggtaaggcccaccgcagctcggtctctgactacgtcaact  
atgatatcatcgccggcattacaactacacggaaagctgaatatcagcgccgacaaggagaa  
cagcattaaactgacctcggtgggttcattctcatctgtgtttatcatctggagaacatc  
tttgtcttgcgtgaccattggaaaaccaagaaattccaccgcacctgtactatttattggca  
atctggccctctcagacctgtggcaggagtgcctacacagctaacctgtttgttgc  
caccacccataagctcactccgcggcgtggttctgcgggaaggagatgtttgtggccctg  
tcagcctccgtttcagttcctcgccatcgccatgtggcgtatcataatgcataatgt  
aactccacaacgggagcaataactccgccttcctgtcaatcagccgtgtggcatctc  
cctcatcctgggtggcctgcctatcatggctggactgcattcgtgcgtgtccagctgtcc  
accgtgtgcgcgtctaccacaaggcactatcatcctttctgcaccacggcttcactctgttc  
tgctctccatcgcatctgtactgcagaatctactccttgcgtcaggactcgagccgcgc  
gacgttccgcaagaacattccaaggccagccgcagctctgagaagtcgtggcgtgtcaag  
accgttaattatcgccctgagcgttcatcgccgtgtggcaccgccttcattgcgttgc  
tggatgtggctgcaaggtaagacactgtgacatccttgcgttgcgttgcgttgc  
agctgtgtcaactccggaccaacccatcattacactctgaccaacaaggagatgcgtcg  
gccttcatccggatcatgtcctgtcaagtgcgcggccgcacggggacgcacccacccagcc  
tgggtcccaagatgagtcctgcaccaccgcagcttcctggccaaggacacttcattcgta  
a

(SEQ ID No. 14)